Respiratory Medicine (2006) **100**, 180–182

respiratoryMEDICINE

SHORT COMMUNICATION

Influence of obstructive sleep apnoea in coronary artery disease: A 10-year follow-up

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Received 5 June 2004; accepted 11 April 2005

KEYWORDS
Obstructive sleep apnoea;
Coronary artery disease;
Mortality

Summary In patients with coronary artery disease (CAD) the prevalence of obstructive sleep apnoea (OSA) is found to be about 14–65%. In this study, the influence of OSA in 50 patients with CAD was prospectively compared during a follow-up period of 10 years. In the follow-up period 4 of 25 patients with OSA and 5 of the 25 without OSA died by cardiovascular complications. The proportion survival curve showed no significant difference for patients with CAD and with versus without OSA. The results of this rather small 10-year follow-up study failed to give further evidence for an increased mortality in patients with CAD and OSA.

Introduction

Mortality from coronary artery disease (CAD) shows a decline attributed to improvements in treatment of CAD and in prevention. Still, the mortality rate remains high in this group of patients. Retrospective studies found an apnoea–hypopnoea index to be an independent predictor for myocardial infarction in obstructive sleep apnoea (OSA).[1–3] The prevalence of OSA is found to be about 14–65% in CAD.[2–6] The first prospective study so far investigating the cardiovascular mortality in CAD patients with versus without concomitant OSA in a 5-year follow-up was published by Peker et al.[7] In this study, OSA, defined as a respiratory disturbance index of 10/h or more was found in 19 of 62 patients. The follow-up revealed an increased risk for untreated OSA of cardiovascular death in patients with CAD.

To confirm this we investigated cardiovascular complications in patients with CAD with versus without OSA in a 10-year follow-up. In our analysis OSA was defined as an apnoea index (AI) >10/h according to study criteria from the previously published prevalence study.[6]

Methods

In the initial overnight study, 50 patients with angiographical provided diagnosis of CAD were

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doi:10.1016/j.rmed.2005.04.009

randomly included (47 men, 3 women; mean age 61+6 years). The selection criteria were an angiographical diagnosed CAD with a stenosis of one or more coronary vessels of at least 50%. A left ventricular ejection fraction of less than 40%, an age of more than 70 years and a history of cerebral infarction were exclusion criteria.[6]

The patients included were primarily investigated by a non-laboratory-monitoring-system (SGT24B, Fa. Jaeger, Wuerzburg, Germany). Twenty-five patients of the included 50 patients showed an AI >10/h with obstructive pattern. The OSA-group had an AI of 19.4+6.7/h compared to an AI of 5.1+2.3/h in the non-OSA-group ($P<0.00001$) (Table 1).

In the baseline OSA-group 19 of the 25 patients participated in a full night polysomnography. In this patient group the AI was 17.0+10.9/h and the apnoea–hypopnoea index was 32.4+16.5/h sleep. Twelve of the 19 polysomnographic controlled patients were recommended to have a continuous positive airway pressure therapy (CPAP). While 5 denied from the beginning, 7 at first tried the therapy option but stopped during the follow-up period. No patient continued CPAP during the complete follow-up period.

For follow-up the patients were contacted and had a request about their medical history during the past time period 10 years after the first sleep study. Those patients that survived and who agreed again were investigated by non-laboratory-monitoring-system for air flow, heart rate, body position and oxygen saturation as well as by echocardiography.

Student's *t*-test or the Mann–Whitney *U*-test were used for variables measured on a continuous scale. Categorical variables were compared by the chi-square test or Fisher exact test (two-tailed). Continuous values are given as mean $\pm$ SD. Survival analyses were performed by the Kaplan–Meier method and statistical comparison by the Log-rank test. A *P* value of 0.05 or less was regarded as statistically significant.

Results

Fifteen patients refused further investigation during the follow-up, but for all patients the history of cardiovascular events and death could be obtained. After a time interval of 10 years 4 patients had died in the OSA-group and 8 in the non-OSA-group. Three patients in the non-OSA-group died due to malignant tumor and 5 due to cardiovascular disease while the 4 patients in the OSA-group died due to cardiovascular disease ($P =$ ns). The proportion of the OSA-group to the non-OSA-group regarding survival time shows no significant increased risk (log-rank test) of cardiovascular complications in OSA-patients ($P =$ ns) (Fig. 1).

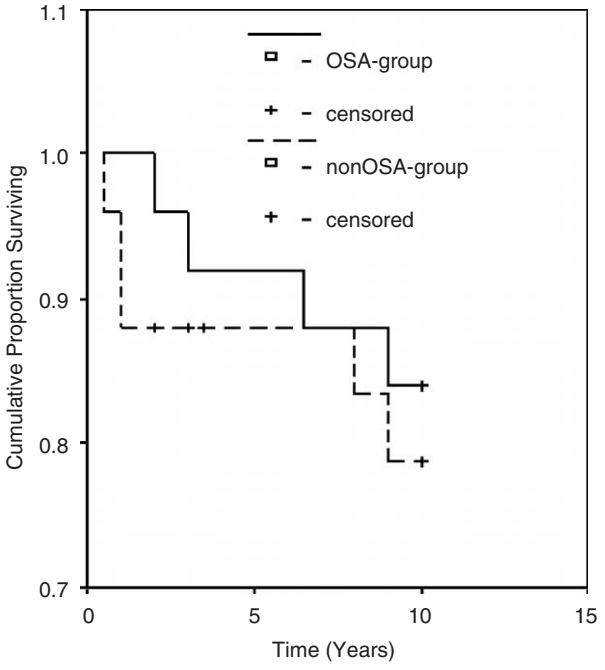

Figure 1 Proportional surviving of OSA versus non-OSA. The figure shows the number of deceased patients during the follow-up period of 10 years. Patients deceased due to malignant diseases were censored.

Table 1 Differences in baseline characteristics from OSA- and non-OSA-patients.

	OSA ($n = 25$)	Non-OSA ($n = 25$)	*P* values
Age (years)	63.1 $\pm$ 3.5	58.4 $\pm$ 7.2	<0.02
BMI (kg/m^2)	27.8 $\pm$ 4.2	25.7 $\pm$ 3.0	<0.05
AI (/h)	19.4 $\pm$ 6.7	5.1 $\pm$ 2.3	<0.00001
Hypertension (*n*)	13	7	<0.05
3-vessel-CAD (%)	20	48	<0.08

BMI = body mass index; AI = apnoea index; 3-vessel-CAD = 3 vessel coronary artery disease; *P* values by Mann–Whitney *U*-test or Chi-squared test.

The number of patients having cardiovascular complications regarding myocardial infarction and cerebral insult during 10-year follow-up were 5 in the initial OSA-group versus 2 in the non-OSA-group ($P = \text{ns}$). Cardiac interventions like catheterization or bypass-surgery where performed in 13 patients of the non-OSA-group and in 11 of the OSA-group ($P = \text{ns}$).

No significant differences were found for initial or follow-up medical treatments between the OSA-group and the non-OSA-group.

For only 26 of the initial 50 patients a follow-up investigation could be performed. From these 26 patients 10 changed their profiles as patients with or without OSA according to study criteria. Seven of those 10 patients had less obstructive apnoeas and only 3 had more than 10/h. These recorded shifts did not result in significant differences for surviving proportion.

Discussion

The first prospective investigation of the impact of OSA on cardiovascular mortality was performed by Peker et al.[7] In Peker's study cardiovascular mortality could be independently related to the respiratory disturbance index. Mooe and colleagues also showed a correlation of an oxygen desaturation index of >5/h in sleep disordered breathing to increased cardiac risk in a 5-year follow-up.[1] This was in concordance with the results of earlier retrospective studies.[2,8,9] In our investigation the number of patients included in the study was small, but this is the first follow-up for a 10-year period. According to our results the influence of OSA does not appear to be a factor explaining an increased mortality in CAD. Although cofactors like body-mass index, hypertension and age have not been matched for both OSA- and non-OSA-patients in the initial study population as listed above there was no significant difference for cardiovascular mortality. In concordance with our findings an AHI >10/h has also been missing significance in primary end point in the 408 patients of Mooe's study population.[1] Mooe and coworkers did not distinguish the different apnoea types. A possible reason in our study may have been the different severity of CAD in both groups with a tendency to more severe CAD in the initial non-OSA-group ($P = 0.08$). In Mooe's study population poor left ventricular function was more common in patients with sleep disordered breathing.[1]

As we performed a second evaluation for sleep apnoea in 26 of the initial study patients an interesting aspect of this study is the high rate of group shifts from OSA to non-OSA and vice versa. Ten of the 26 patients with a second investigation changed their status, mainly from OSA to non-OSA. These recorded shifts did not result in significant differences for surviving proportion.

For the initial medical treatment a significant rise in cardiac medications during follow-up can be stated. Since the start of modifications in medication was not referred during follow-up there is no way to emphasize possible interferences in the 10 years of follow-up. In the study population of Peker and coworkers the patients with OSA tended to use more cardiac medications. This could have been reasoned by a more severe cardiac failure in the OSA-group. Echocardiographic data of the patients in Peker's study were not completely obtained so severity of cardiac failure cannot be definitively stated.

In conclusion, we missed a significant influence of OSA in CAD in our small patient group although the evidence of an influence is growing due to several investigations.[1,3,7] Possibly, the relationship has been overemphasized in previous studies. Still a prospective and adequate sample sized study with matched patient groups for severity of heart disease has to be performed.

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